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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,578	03/09/2001	Patrick Hwu	2026-4341	6841

23460 7590 01/31/2003

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/31/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/803,578	Hwu et al.
Examiner	**Art Unit**
Michael C. Wilson	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *9-9-02 and 10-22-02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above, claim(s) *5, 9, 14, and 16-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6-8, 10-13, 15, and 40-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group I in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the examiner has not alleged that there would be an undue burden on Examiner to examine any of the Groups together and because Groups I and II and Groups III and IV are classified the same. This is not found persuasive. The burden required to search for all cells encompassed by the claims would be undue because the lymphocytes of Groups I and II have different structures as set forth in the restriction requirement. In addition, Groups I and II are not used together and have different modes of operation as set forth in the restriction. Groups I and III are patentably distinct because the product of group I can be used *in vitro* for assays or *in vivo* for treatment which are patentably distinct methods. Groups I and IV are patentably distinct because lymphocytes specific for tumor antigens are and viral antigens are not disclosed as being used together and have different modes of operation. The multitude of chimeric receptors and antigens encompassed by the claims would be undue to search and examine together.

The requirement is still deemed proper and is therefore made FINAL.

Claims 5, 9, 14 and 16-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Applicants state claims 1, 3, 4, 6, 7, 10, 40-42 are readable on the elected species. However, claims 1-4, 6-8, 10-13, 15 and 40-43 are all readable on the elected species because the limitations in claims 2, 8, 11-13 and 43 do not exclude ovarian tumor antigens and Mov-γ as elected.

Claims 1-4, 6-8, 10-13, 15 and 40-43 are under consideration in the instant office action as they relate to lymphocytes having a chimeric receptor that is Mov-γ or a T-cell receptor (TCR) reactive with an ovarian tumor antigen and a TCR reactive with a "strong antigen" (claim 1), a lymphocyte having a TCR reactive with an allogeneic agent and a Mov-γ reactive with an ovarian tumor antigen (claim 11), a lymphocyte having a T-cell receptor reactive with a "strong" antigen and an Mov-γ reactive with an ovarian tumor antigen (claim 12), a pharmaceutical composition comprising lymphocytes having an Mov-γ reactive with an ovarian tumor antigen and "preselected" for reactivity with a "strong" antigen (claim 40), and a method of making lymphocytes comprising selecting lymphocytes that react with a "strong" antigen *ex vivo*, transducing the lymphocytes with an Mov-γ that is reactive with an ovarian tumor antigen.

Specification

1. The disclosure is objected to because of the following informalities: the status of application 08/547263 cited on pg 17, line 5, needs updated. Correction will be required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-4, 6-8, 10-13, 15 and 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 40 are indefinite because it is unclear how the term "preselected" further limits the lymphocytes being claimed. The distinction between a "preselected" lymphocyte population transfected with Mov-γ and any other lymphocyte population transfected with Mov-γ cannot be determined. It is unclear to what the "selection" is prior ("pre").

The metes and bounds of an "endogenous T-cell receptor reactive with a preselected strong antigen" are unclear (claim 1). It is unclear how the "strong antigen" recognized by the endogenous receptor correlates to the "tumor antigen" recognized by the chimeric receptor. The metes and bounds of a "strong antigen" cannot be determined. How strong is a "strong antigen?" Does the immune response to the antigen have to a particular type of response or can it be any immune response?

The metes and bounds of a "strong antigen" that is an "allogeneic agent" is unclear (claim 2). The metes and bounds of "allogeneic agent" cannot be determined as the phrase is not defined in the specification and does not have an art accepted meaning. It is unclear to what the

agent or "strong antigen" are allogeneic as allogeneic is a relative term used to describe the histocompatibility between two things.

Claim 4 is indefinite because it does not clearly set forth the tumor antigen is an ovarian tumor antigen. The metes and bounds of tumor antigens "derived" from ovarian tumors is indefinite.

Claim 8 is indefinite because it is unclear to what the peripheral blood cells are "allogeneic."

Claim 8 is indefinite because it is unclear how a "strong antigen" can comprise peripheral blood cells. Antigens are protein and do not comprise cells as claimed. The metes and bounds of which cells that are "strong antigens" as claimed is unclear.

The metes and bounds of the term "Mov-γ" in claim 10 is unclear. It is unclear if the term is generic to any chimeric receptor having a variable region of a monoclonal antibody and a T-cell receptor γ chain (pg 8, line 4) or if it is limited to a chimeric receptor having a variable region of a monoclonal antibody and a T-cell receptor γ chain that is specific to ovarian tumor antigen (pg 27, line 2).

The metes and bounds of the cells encompassed by claim 11 is unclear. It unclear to what the agent is "allogeneic." The term is allogeneic is a relative term; however, it is unclear if the agent is allogeneic to the lymphocyte or T-cell receptor. It is also unclear how the "allogeneic agent" relates to the "tumor antigen." Do the T-cell receptor and chimeric receptors recognize the same antigen?

The metes and bounds of antigens that are "strong antigens" in claim 12 cannot be determined as the phrase is not defined in the specification and does not have an art accepted meaning. Nor are the metes and bounds of what applicants consider "strong" antigens defined in the specification. It is unclear if the immune response to the antigen is limited to a particular immune response or if it can be any immune response.

It is unclear how the "tumor antigen" and "strong antigen" in claim 12 relate. It is unclear if they are different antigens or the same antigen. Do both receptors recognize the same antigen?

The phrase "can be activated *in vivo* with the strong antigen" (claim 12) is unclear because it does not clearly set forth a function of the lymphocytes or alter the structure of the lymphocyte. It is unclear if the lymphocytes claimed are *in vitro* or *in vivo*. It is unclear if the "strong antigen" is administered or if it is already present *in vivo*.

The metes and bounds of the cells encompassed by claim 13 is unclear. It unclear to what the agent is "allogeneic." The term is allogeneic is a relative term; however, it is unclear if the agent is allogeneic to the lymphocyte, the chimeric receptor or the T-cell receptor. It is also unclear how the "allogeneic agent" relates to the "tumor antigen." Do the T-cell receptor and chimeric receptors recognize the same antigen?

The metes and bounds of the cells encompassed by claim 15 is unclear. It unclear to what the agent is "allogeneic." The term is allogeneic is a relative term; however, it is unclear if the agent is allogeneic to the lymphocyte, chimeric receptor or T-cell receptor. It is also unclear how the "allogeneic agent" relates to the "tumor antigen." Do the T-cell receptor and chimeric

receptors recognize the same antigen? It is unclear how peripheral blood cells can be antigens (as in parent claim 13). It is unclear how the term "donor" limits the claim because the claims do not have a donor.

The metes and bounds of "strong antigen" are unclear (claims 40-42). It is unclear how the "strong antigen" correlates to the "tumor antigen" recognized by the chimeric receptor. The metes and bounds of a "strong antigen" cannot be determined. How strong is a "strong antigen?" Does the immune response to the antigen have to a particular type of response or can it be any immune response?

The metes and bounds of cells "preselected" for reactivity is unclear because it does not clearly set forth the function of the cells claimed (claim 41). It is unclear if applicants intend to make the claim a product by process claim or if the phrase is a functional limitation of the cell indicating it reacts with an antigen.

The use of "preselected" in claim 41 is indefinite because it is unclear how "preselected" relates to the step of "selecting". Is another step required or is does the selecting step produce "preselected lymphocytes"?

The phrase "dual specificity lymphocytes" is indefinite (claim 41). It unclear to what two things the lymphocytes are specific.

The metes and bounds of the cells encompassed by claim 42 is unclear. It unclear to what the agent is "allogeneic." The term is allogeneic is a relative term; however, it is unclear if the agent is allogeneic to the lymphocyte, chimeric receptor or T-cell receptor. It is also unclear how

the "allogeneic agent" relates to the "tumor antigen." Do the T-cell receptor and chimeric receptors recognize the same antigen?

It is unclear if folate binding protein (FBP) is an ovarian tumor antigen as elected (claim 43). It is unclear how FBP relates to the antigen recognized by the Mov-γ receptor, Mov18, or how it relates to the "strong antigen" throughout the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
>
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
>
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

3. Claims 1-4, 6-8, 10-13, 15 and 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Nishimura (US Patent 5,830,755).

Nishimura taught tumor infiltrating lymphocytes (TIL) transfected with an Mov-γ recognizing ovarian tumors (Mov18) (col. 37, line 54). The TIL are "preselected" and inherently have an "endogenous T-cell receptor reactive with a strong antigen" as claimed because they

were stimulated *in vitro* with antigen (col. 36, line 38-57, especially line 44) and because the metes and bounds of "strong" antigens is unclear (see 112/2nd). Claims 2, 3, 8, 12, 13, 15 and 43 are included because the metes and bounds of the claims (e.g. allogeneic) are unclear.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL C. WILSON
PATENT EXAMINER